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10/057,247	01/25/2002	Ethan Lerner	10287-066001 / 1791.1	2777

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FISH & RICHARDSON PC  
225 FRANKLIN ST  
BOSTON, MA 02110

EXAMINER
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KIM, JENNIFER M

ART UNIT	PAPER NUMBER
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1617

DATE MAILED: 06/18/2003

8

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/057,247

Applicant(s)

LERNER ET AL.

Examiner

Jennifer Kim

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 08 April 2003.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-22 is/are pending in the application.
- 4a) Of the above claim(s) 13-17 and 23-27 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-5, 7-11, 18 and 20-22 is/are rejected.
- 7) ☒ Claim(s) 6, 12 and 19 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

## **DETAILED ACTION**

Applicants' election without traverse of Group I, claims 1-12 and 18-22, drawn to a method of preventing or treating a wrinkle in a subject comprising administering an inhibitor of nitric oxide synthase (NOS) in Paper No. 7 is acknowledged. Accordingly, claims 13-17 and 23-27 are withdrawn from consideration since they are non-elected invention.

### **Claim objection**

Claims 1-12 and 18-22 are objected to because of the following informalities: The recitation of the treatment of individuals "in need" of the treatment of a certain condition is missing. Appropriate correction is required. A physician will typically examine many patients with various pathologies, and only some will have a particular disease requiring a particular treatment. It has been traditional in United States practice to recite the treatment of individuals "in need" of the treatment of a certain condition so as to indicate that particular subset of patients actually in need of intervention; an alternative is to recite the treatment of an individual "suffering from" a given disease. Accordingly, the following format is preferred for claiming methods of treating: "A method for treating disease X comprising administering to an individual suffering from/in need of such treatment an effective amount of agent Y". Claims not specifying the subset of patients to be treated in this manner are generally viewed as being anticipated by any prior art

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method using a given agent since they read on administration to the general population and not a specified subset requiring treatment.

***Claim Rejections - 35 USC § 112***

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-6, 8-15, and 17-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the "treatment of a wrinkle comprising administering L-NAME", does not reasonably provide enablement for the "prevention of a wrinkle" or "treatment of a wrinkle comprising administering any NOS inhibitor. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

3. Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, predictability of the prior art, state of the prior art and the amount of experimentation necessary. All of the **Wands factors** have been considered with regard to the instant claims, with the most relevant factors discussed below.

***Nature of the Invention:*** All of the rejected claims are drawn to a method of treating or preventing a wrinkle or treating a wrinkle comprising administering any NOS inhibitor in a subject with an amount sufficient to produce or "prevent" or treat said wrinkle comprising administering **any** nitric oxide synthase. The nature of the invention is extremely complex in that it encompasses the **actual prevention** or treatment of a wrinkle such that the subject treated with any of above compounds does not contract wrinkles.

***Breath of the Claims:*** The complex of nature of the claims greatly exacerbated by breath of the claims. The claims encompass prevention of a wrinkles or treatment of a wrinkles with a NOS inhibitor in a subject which has potentially many different causes (i.e. many different skin disorders or combination of skin disorder, aging or natural nature of the skin). Each of which may or may not be addressed by the administration of the claimed compound.

***Guidance of the Specification:*** The guidance given by the specification as to how one would administered the claimed compounds to a subject in order to actually prevent wrinkle is minimal. All of the guidance provided by the specification is directed towards treatment rather than prevention of wrinkles. The guidance only provide by the specification directed towards administration of specific NOS inhibitor (i.e. L-NAME) rather than any NOS inhibitor.

***Working Examples:*** All of the working examples provided by the specification are directed toward the treatment employing specific NOS inhibitor (i.e. L-NAME)

rather than any NOS inhibitors. The working examples provided by the specification are directed toward the treatment rather than prevention of wrinkles.

**State of the Art:** While the state of the art is relatively high with regard to treatment of wrinkles (i.e. wrinkles caused by aging), the state of the art with regard to prevention of such condition is underdeveloped. In particular, there do not appear to be any examples or teachings in the prior art wherein a compound similar to the claimed compounds was administered to a subject to **prevent development of wrinkles**. The state of the art is relatively high with regard to treatment of wrinkles with certain NOS inhibitor (aminoguanidine), the state of the art with regard to treatment of wrinkles regard to all class of NOS inhibitor is underdeveloped.

**Predictability of the Art:** The lack of significant guidance from the specification or prior art with regard to the actual prevention of wrinkles in a human subject with the claimed compounds and the lack of significant guidance from the specification or prior art with regard to the actual treatment of wrinkles employing any NOS inhibitor makes practicing the claimed invention unpredictable in terms of prevention of development of wrinkles and treatment of wrinkles employing any NOS inhibitor.

**The amount of Experimentation Necessary:** In order to practice claimed invention, one of skilled in the art would have to first envision a combination of appropriate pharmaceutical carrier, compound dosage, duration of treatment, route of administration, etc. and appropriate animal model system for one of the

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claimed compounds and test the combination in the model system to determine whether or not the combination is effective for treatment or prevention of development of wrinkles. If unsuccessful, which is likely given the lack of significant guidance from the specification or prior art regard prevention of wrinkles with any compound, one of skill in the art would have to then either envision a modification of the first combination of pharmaceutical compound, compound dosage, duration of treatment, route of administration, etc. and appropriate animal model system, or envision an entirely new combination of the above, and test the system again. If again unsuccessful, which is likely given the lack of significant guidance form the specification of prior art regarding prevention of wrinkles with any compound, the entire, unpredictable process would have to be repeated until successful. Therefore, it would require undue, unpredictable experimentation to practice the claimed invention to prevent the development of wrinkles in a subject by administration of one of the claimed compounds.

Therefore, a method of preventing or treating in a subject in development of wrinkles administering a NOS inhibitor is not considered to be enabled by the instant specification.

***Claim Rejections - 35 USC § 103***

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The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5, 7-11, 18 and 20-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cerami et al. (U.S. Patent No. 6,114,323).



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Cerami et al. teach aminoguanidine (NOS inhibitor) can be topically applied for treatment of wrinkling of skin. (column 4, lines 2-4, column 5, lines 30-38 and column 9, lines 6-11).

Cerami et al. do not teach the caused of the wrinkle set forth in claim 8, the type of the wrinkle set forth in claims 9 and 20, a formulation technique set forth in claims 5,11 and the directions how to apply set forth in claim 21.

It would have been obvious to one of ordinary skill in the art to employ aminoguanidine (NOS inhibitor) for the treatment of wrinkle because Cerami et al. teach that aminoguanidine can be use for the treatment of wrinkling of skin. One would have been motivated to employ aminoguanidine for the treatment of skin wrinkle to achieve the expected therapeutic benefit in wrinkle treatment of aminoguanidine.

The type of the wrinkle set forth in claims 9 and 20, a formulation technique set forth in claims 5,11 and the directions how to apply set forth in claim are all deemed obvious since they are all within the knowledge of the skilled pharmacologist and represent conventional formulations and modes of administration. Further, one of ordinary skill in the art would be obvious to employ aminoguanidine in any wrinkled skin regardless of the cause since Cerami et al. teach that aminoguanidine is effective for any wrinkled skin in general.

For these reasons the claimed subject matter is deemed to fail to patentably distinguish over the state of the art as represented by the cited references. The claims are therefore properly rejected under 35 U.S.C. 103.

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***Allowable Subject Matter***


Claims 6, 12 and 19 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Kim whose telephone number is 703-308-2232. The examiner can normally be reached on Monday through Friday 8:30am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 703-305-1877. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

RUSSELL TRAVERS  
PRIMARY EXAMINER  
GROUP 1200

 Theodore J. Criares  
Primary Examiner  
Art Unit 1617

jmk  
June 16, 2003